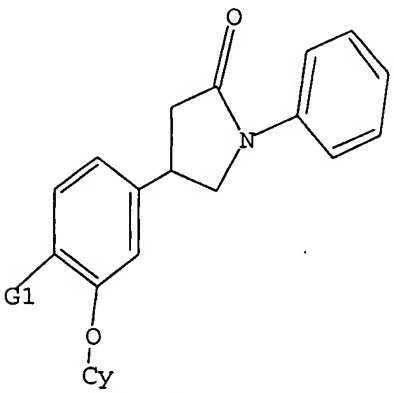
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-18 14-15 15-16 16-17 17-18

G1:H,X,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,PhO,CN,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 21:CLASS
22:CLASS 23:Atom

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 H,X,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,PhO,CN,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 13:32:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9736 TO ITERATE

100.0% PROCESSED 9736 ITERATIONS 462 ANSWERS
SEARCH TIME: 00.00.01

L2 462 SEA SSS FUL L1

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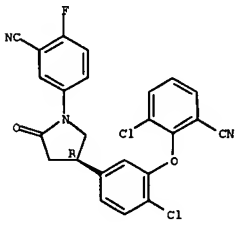
L2 ANSWER 1 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-13-5 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 3-chloro-2-[2-chloro-5-[(3R)-1-(3-cyano-4-fluorophenyl)-5-oxo-3-pyrrolidinyl]phenoxy]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H14 Cl2 F N3 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



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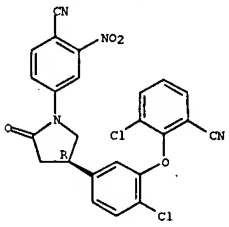
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-10-2 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 3-chloro-2-[2-chloro-5-[(3R)-1-(4-cyano-3-nitrophenyl)-5-oxo-3-pyrrolidinyl]phenoxy]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H14 Cl2 N4 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

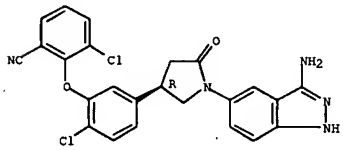


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-09-9 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 2-[5-[(3R)-1-(3-amino-1H-indazol-5-yl)-5-oxo-3-pyrrolidinyl]-2-chlorophenoxy]-3-chloro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H17 Cl2 N5 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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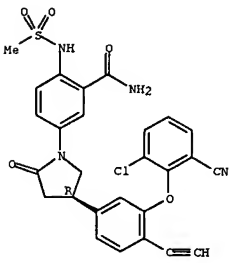
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 4 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-08-8 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H21 Cl N4 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

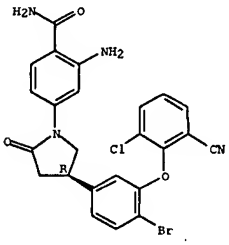


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 5 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-07-7 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 2-amino-4-[(4R)-4-[4-bromo-3-(2-chloro-6-cyanophenoxy)phenyl]-2-oxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H18 Br Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

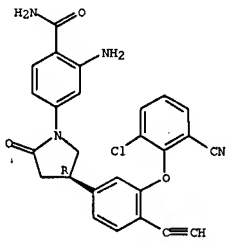


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 6 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-06-6 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 2-amino-4-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H19 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

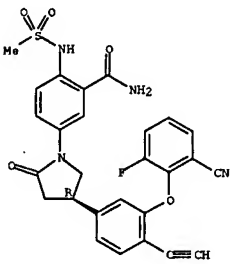


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 7 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-05-5 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-cyano-6-fluorophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H21 F N4 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

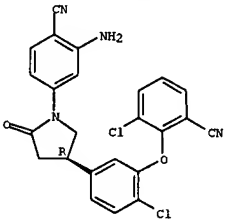


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 8 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-04-4 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 2-[5-[(3R)-1-(3-amino-4-cyanophenyl)-5-oxo-3-pyrrolidinyl]-2-chlorophenoxy]-3-chloro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H16 Cl2 N4 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

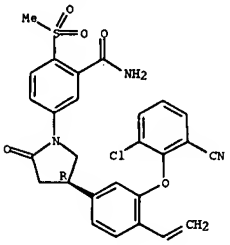


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 9 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-03-3 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethenylphenyl]-2-oxo-1-pyrrolidinyl]-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H22 Cl N3 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
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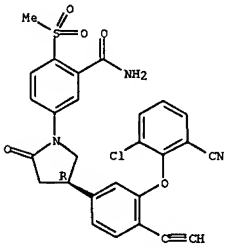
L2 ANSWER 10 OF 462 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-02-2 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H20 Cl N3 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   193.40     196.34

FILE 'CAPLUS' ENTERED AT 13:33:38 ON 20 APR 2007
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FILE LAST UPDATED: 19 Apr 2007  (20070419/ED)

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L3             8 L2

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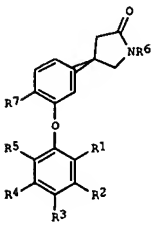
L3 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:768981 CAPLUS
DOCUMENT NUMBER: 145:188711
TITLE: Preparation of phenoxyphenylpyrrolidones for treatment of HIV infection.
INVENTOR(S): Wu, Baogen; Nguyen, Truc N.; Ellis, David A.; He, Xiaohui; Anaclerio, Beth M.; Yang, Kunyong; Choi, Ha-Soon; Wang, Zhicheng; Marsilje, Thomas; He, Yun
PATENT ASSIGNEE(S): IRM LLC, Bermuda
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006081554	A2	20060803	WO 2006-US3217	20060130
WO 2006081554	A3	20061214		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-648027P P 20050128
OTHER SOURCE(S): MARPAT 145:188711
GI



I

AB Title compds. [I; R1, R5 = H, cyano, halo, (substituted) alkyl, alkenyl, OR8; R8 = (substituted) alkyl, haloalkyl; R2, R4 = H, halo, cyano, (substituted) alkyl; R3 = H, cyano, alkyl; R6 = fused Ph heterocyclyl,

L3 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pyridine N-oxide, pyridyl, pyridone, (substituted) Ph; R7 = halo, alkyl, alkenyl, alkynyl], were prepd. as inhibitors of HIV in cells (no data). Thus, 3-amino-5-[4-[4-chloro-3-(2-chloro-6-cyanophenoxy)phenyl]-2-oxopyrrolidin-1-yl]indazole-1-carboxamide was prepd. in many steps.

L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:499083 CAPLUS
DOCUMENT NUMBER: 145:167034
TITLE: Synthesis and evaluation of N-aryl pyrrolidinones as novel anti-HIV-1 agents. Part 1
AUTHOR(S): Wu, Baogen; Kuhen, Kelli; Ngoc Nguyen, Truc; Ellis, David; Anaclerio, Beth; He, Xiaohui; Yang, Kunyong; Karanewsky, Donald; Yin, Hong; Wolff, Karen; Bieza, Kimberly; Caldwell, Jeremy; He, Yun
CORPORATE SOURCE: Genomics Institute of the Novartis Research Foundation (GNF), San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(13), 3430-3433
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:167034
AB The synthesis and preliminary structure-activity relationship of a series of pyrrolidinones are described. These pyrrolidinones have been characterized as novel non-nucleoside reverse transcriptase inhibitors (NNRTIs) which are highly potent against wild-type and drug-resistant human immunodeficiency viruses (HIV-1).
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1043376. CAPLUS
DOCUMENT NUMBER: 142:168960
TITLE: On the role of polarizability in QSAR
AUTHOR(S): Verma, Rajeshwar P.; Kurup, Alka; Hansch, Corwin
CORPORATE SOURCE: Department of Chemistry, Pomona College, Claremont, CA, 91711, USA
SOURCE: Bioorganic & Medicinal Chemistry (2004), Volume Date 2005, 13(1), 237-255
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The polarizability of a mol., an important phys. property, is currently attracting our attention particularly in the area of QSAR for chemical-biol. interactions. In this report, the polarizability effects on ligand-substrate interactions has been discussed in terms of NVE (number of valence electrons) using additive values for valence electrons and the formulation of a total number of 51 QSAR. The QSAR model can be illustrated by Eq. I. log 1/C = a(NVE) + constant
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:370899 CAPLUS
DOCUMENT NUMBER: 140:391194
TITLE: Preparation of pyrrolidones with anti-HIV activity
INVENTOR(S): Wu, Baogen; He, Yun; Nguyen, Truc; Kuhen, Kelli L.; Ellis, David Archer; Jiang, Tao
PATENT ASSIGNEE(S): IRM LLC, Bermuda
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

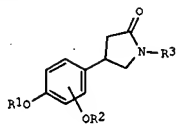
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037784	A2	20040506	WO 2003-US33560	20031021
WO 2004037784	A3	20040819		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003285952	A1	20040513	AU 2003-285952	20031021
US 2004157859	A1	20040812	US 2003-690873	20031021
PRIORITY APPLN. INFO.:			US 2002-420480P	P 20021021
			US 2002-422619P	P 20021030
			WO 2003-US33560	W 20031021

OTHER SOURCE(S): MARPAT 140:391194
GI

L3 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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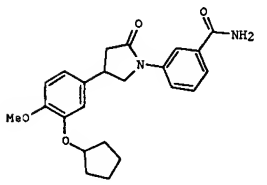


II

AB The present invention relates to inhibition of viruses, e.g., HIV using pyrrolidones I and compds. related to pyrrolidones I [R1 = H, alkyl, cycloalkyl; R2 = (un)substituted Ph, CH2Ph, cycloalkyl; R3 = (un)substituted pyridyl, pyrimidinyl, pyrazinyl, Ph]. The invention further relates to methods for identifying and using agents, including small mol. chemical compns. that inhibit HIV replication in a cell, as well as to methods of prophylaxis, and therapy related to HIV infection and related disease states such as AIDS. Preparation of the compds. I is described in 28 synthetic examples. Thus, reacting 4-(3-cyclopentyloxy-4-methoxyphenyl)-pyrrolidin-2-one with 3-bromobenzonitrile in the presence of potassium phosphate and trans-1,2-cyclohexanediamine in DMF/dioxane followed by treating a solution of the resulting benzonitrile with 25% NaOH solution, and then with 35% H2O2 afforded II.

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

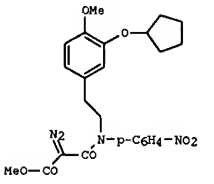
ACCESSION NUMBER: 2001:584505 CAPLUS
DOCUMENT NUMBER: 135:344336
TITLE: Synthesis and structure-activity relationship of N-arylrolipram derivatives as inhibitors of PDE4 isozymes
AUTHOR(S): Keller, Thomas H.; Bray-French, Katharine; Demnitz, F. W. Joachim; Muller, Thomas; Pombo-Villar, Esteban; Walker, Christoph
CORPORATE SOURCE: Respiratory Disease Therapeutic Area, Novartis Horsham Research Center, West Sussex, RH12 5AB, UK
SOURCE: Chemical & Pharmaceutical Bulletin (2001), 49(8), 1009-1017
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:344336

AB Structure activity studies of N-phenylrolipram derivs. led to the identification of highly potent PDE4 inhibitors. The potential of these inhibitors for cellular activity was routinely assessed in an assay of fMLP induced oxidative burst in human eosinophils. Since 1st generation PDE4 inhibitors were plagued with a number of unwanted side effects, parallel structure activity studies for competition with the [3H]-rolipram binding site in rat brain were performed. In this fashion 5-[4-(3-cyclopentyloxy-4-methoxyphenyl)-2-oxopyrrolidin-1-yl]-3-(3-methoxybenzyloxy)benzoic acid N',N'-dimethylhydrazide was identified as a potent inhibitor of PDE4 which exhibits >1000 fold selectivity vs. PDE3, and is a nanomolar inhibitor in all the cellular assays tested. Studies on the stereoselectivity of PDE4 inhibition of this class of rolipram based compds. revealed, that for example (S)-4-(3-cyclopentyloxy-4-methoxyphenyl)-1-[-3-(3-methoxybenzyloxy)phenyl]pyrrolidin-2-one is a more potent inhibitor than the (R)-enantiomer. This effect can also be observed in primary human cells where the (S)-enantiomer is .apprx.10 fold more potent than the corresponding (R)-enantiomer.

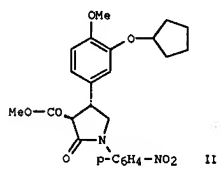
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:726410 CAPLUS
DOCUMENT NUMBER: 132:122469
TITLE: Catalytic enantioselective synthesis of the phosphodiesterase type IV inhibitor (R)-(-)-rolipram via intramolecular C-H insertion process
AUTHOR(S): Anada, Masahiro; Mita, Orie; Watanabe, Hiroko; Kitagaki, Shinji; Hashimoto, Shunichi
CORPORATE SOURCE: Graduate School Pharmaceutical Sciences, Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Synlett (1999), (11), 1775-1777
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:122469
GI



I



II

AB A new route to (R)-(-)-rolipram was developed, wherein the key step relies on enantioselective intramol. C-H insertion of N-alkyl-N-(4-nitrophenyl)-α-(methoxycarbonyl)-α-diazoacetamide I catalyzed by a chiral dirhodium(II) complex. A dirhodium(II) carboxylate incorporating N-benzene-fused (S)-phthaloyl-tert-leucinate as a bridging ligand proved to be the catalyst of choice for this process, providing the desired 2-pyrrolidinone II in 88% ee.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:11369 CAPLUS
DOCUMENT NUMBER: 130:153528
TITLE: Synthesis of N-arylrolipram derivatives - potent and selective phosphodiesterase-IV inhibitors - by copper catalyzed lactam-aryl halide coupling
AUTHOR(S): Aebischer, Esther; Bacher, Edmond; Demnitz, F. W. Joachim; Keller, Thomas H.; Kurzmeyer, Miriam; Ortiz, Marta L.; Pombo-Villar, Esteban; Weber, Hans-Peter
CORPORATE SOURCE: NOVARTIS Pharma AG, Preclinical Research, Basel, CH-4002, Switz.
SOURCE: Heterocycles (1998), 48(11), 2225-2229
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:153528
AB The copper catalyzed coupling of rolipram with a wide variety of aryl halides affords N-arylrolipram derivs., potent and selective phosphodiesterase type-IV inhibitors.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:1280 CAPLUS
DOCUMENT NUMBER: 130:177372
TITLE: N-Arylrolipram derivatives as potent and selective PDE4 inhibitors
AUTHOR(S): Bacher, Edmond; Boer, Christiene; Bray-French, Katharine; Demnitz, F. W. Joachim; Keller, Thomas H.; Mazzoni, Lazzaro; Muller, Thomas; Walker, Christoph
CORPORATE SOURCE: Respiratory Disease Therapeutic Area, Novartis Horsham Research Center, West Sussex, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(22), 3229-3234
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Derivatization of rolipram led to the identification of 3-[4-(3-cyclopentyloxy-4-methoxyphenyl)-2-oxo-pyrrolidin-1-yl]-5-(3-methoxybenzyloxy)benzoic acid N',N'-dimethylhydrazide, a potent and selective inhibitor of PDE4, which inhibits the activation of human leukocytes with pIC50 values in the range of 7.3-7.8, and blocks antigen-induced eosinophilia in Brown Norway rats at a dose of 1 mg/kg.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        28.28     224.62

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                        -6.24      -6.24

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DICTIONARY FILE UPDATES:  19 APR 2007  HIGHEST RN 931104-30-2

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http://www.cas.org/ONLINE/UG/regprops.html

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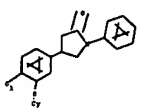

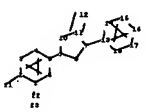

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ring nodes :
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ring bonds :
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15-16 16-17 17-18
exact/norm bonds :
1-22 2-21 7-8 7-11 7-13 8-9 9-10 10-11 11-12 22-23
exact bonds :
5-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-18 14-15 15-16 16-17 17-18

G1:H,X,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,PhO,CN,Ak

Hydrogen count :
8:>= minimum 2 10:>= minimum 2
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 21:CLASS
22:CLASS 23:Atom

L4 STRUCTURE UPLOADED

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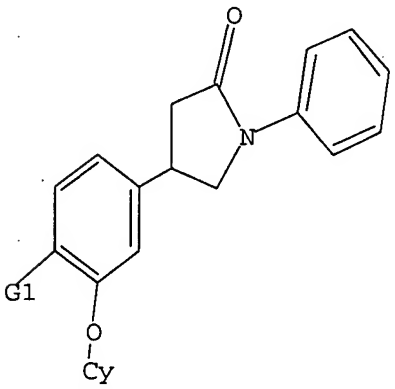
L4 STR



G1 H,X,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,PhO,CN,Ak

Structure attributes must be viewed using STN Express query preparation.

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FULL SEARCH INITIATED 13:41:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9736 TO ITERATE

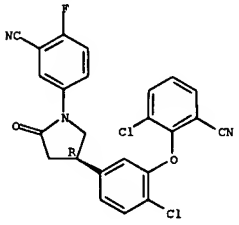
100.0% PROCESSED 9736 ITERATIONS 461 ANSWERS
SEARCH TIME: 00.00.01

L5 461 SEA SSS FUL L4

=> d l5 1-10

L5 ANSWER 1 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-13-5 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 3-chloro-2-[2-chloro-5-[(3R)-1-(3-cyano-4-fluorophenyl)-5-oxo-3-pyrrolidinyl]phenoxy]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H14 Cl2 F N3 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

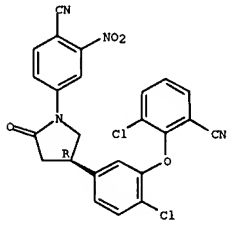


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 2 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-10-2 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 3-chloro-2-[2-chloro-5-[(3R)-1-(4-cyano-3-nitrophenyl)-5-oxo-3-pyrrolidinyl]phenoxy]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H14 Cl2 N4 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

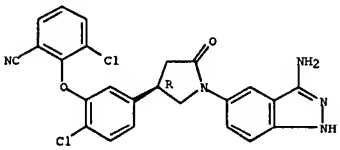


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 3 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-09-9 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 2-[5-[(3R)-1-(3-amino-1H-indazol-5-yl)-5-oxo-3-pyrrolidinyl]-2-chlorophenoxy]-3-chloro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H17 Cl2 N5 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

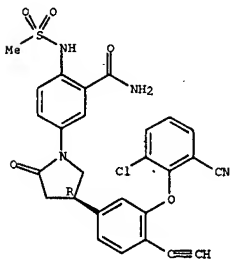


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 4 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-08-8 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H21 Cl N4 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

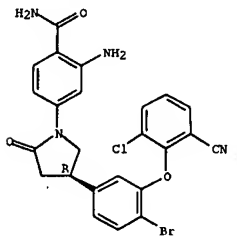


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 5 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-07-7 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 2-amino-4-[(4R)-4-[4-bromo-3-(2-chloro-6-cyanophenoxy)phenyl]-2-oxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H18 Br Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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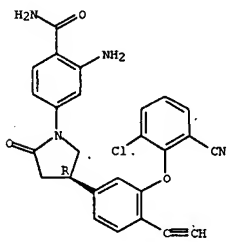
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 6 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-06-6 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 2-amino-4-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H19 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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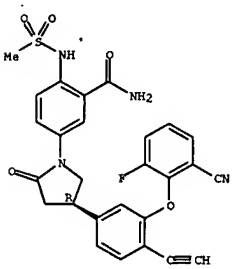
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 7 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-05-5 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-cyano-6-fluorophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H21 F N4 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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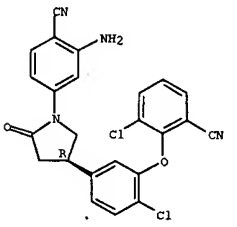
L5 ANSWER 8 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-04-4 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 2-[5-[(3R)-1-(3-amino-4-cyanophenyl)-5-oxo-3-pyrrolidinyl]-2-chlorophenoxy]-3-chloro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H16 Cl2 N4 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

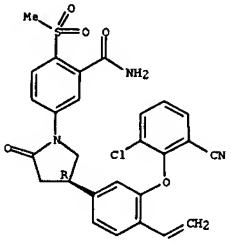


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 9 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-03-3 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethenylphenyl]-2-oxo-1-pyrrolidinyl]-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H22 Cl N3 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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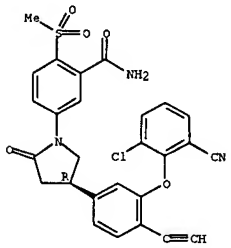
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 10 OF 461 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-02-2 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H20 Cl N3 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



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FILE LAST UPDATED: 19 Apr 2007  (20070419/ED)

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L6            8 L5

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L6 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:760981 CAPLUS
DOCUMENT NUMBER: 145:188711
TITLE: Preparation of phenoxyphenylpyrrolidones for treatment of HIV infection.
INVENTOR(S): Wu, Baogen; Nguyen, Truc N.; Ellis, David A.; He, Xiaohui; Anaclerio, Beth M.; Yang, Kunyong; Choi, Ha-Soon; Wang, Zhicheng; Marsilje, Thomas; He, Yun
PATENT ASSIGNEE(S): IRM LLC, Bermuda
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006081554	A2	20060803	WO 2006-US3217	20060130
WO 2006081554	A3	20061214		

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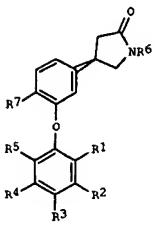
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-648027P P 20050128
OTHER SOURCE(S): MARPAT 145:188711
GI



I

AB Title compds. [I; R1, R5 = H, cyano, halo, (substituted) alkyl, alkenyl, OR8; R8 = (substituted) alkyl, haloalkyl; R2, R4 = H, halo, cyano, (substituted) alkyl; R3 = H, cyano, alkyl; R6 = fused Ph heterocyclyl,

L6 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pyridine N-oxide, pyridyl, pyridone, (substituted) Ph; R7 = halo, alkyl, alkenyl, alkynyl], were prepd. as inhibitors of HIV in cells (no data). Thus, 3-amino-5-[4-[4-chloro-3-(2-chloro-6-cyanophenoxy)phenyl]-2-oxopyrrolidin-1-yl]indazole-1-carboxamide was prepd. in many steps.

L6 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:499083 CAPLUS
DOCUMENT NUMBER: 145:167034
TITLE: Synthesis and evaluation of N-aryl pyrrolidinones as novel anti-HIV-1 agents. Part 1
AUTHOR(S): Wu, Baogen; Kuhen, Kelli; Ngoc Nguyen, Truc; Ellis, David; Anaclerio, Beth; He, Xiaohui; Yang, Kunyong; Karanewsky, Donald; Yin, Hong; Wolff, Karen; Bieza, Kimberly; Caldwell, Jeremy; He, Yun
CORPORATE SOURCE: Genomics Institute of the Novartis Research Foundation (GNF), San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(13), 3430-3433
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:167034
AB The synthesis and preliminary structure-activity relationship of a series of pyrrolidinones are described. These pyrrolidinones have been characterized as novel non-nucleoside reverse transcriptase inhibitors (NNRTIs) which are highly potent against wild-type and drug-resistant human immunodeficiency viruses (HIV-1).
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

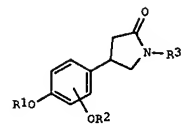
L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1043376 CAPLUS
DOCUMENT NUMBER: 142:168960
TITLE: On the role of polarizability in QSAR
AUTHOR(S): Verma, Rajeshwar P.; Kurup, Alka; Hansch, Corwin
CORPORATE SOURCE: Department of Chemistry, Pomona College, Claremont, CA, 91711, USA
SOURCE: Bioorganic & Medicinal Chemistry (2004), Volume Date 2005, 13(1), 237-255
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The polarizability of a mol., an important phys. property, is currently attracting our attention particularly in the area of QSAR for chemical-biol. interactions. In this report, the polarizability effects on ligand-substrate interactions has been discussed in terms of NVE (number of valence electrons) using additive values for valence electrons and the formulation of a total number of 51 QSAR. The QSAR model can be illustrated by Eq. I. log 1/C = a(NVE) ± constant
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:370899 CAPLUS
DOCUMENT NUMBER: 140:391194
TITLE: Preparation of pyrrolidones with anti-HIV activity
INVENTOR(S): Wu, Baogen; He, Yun; Nguyen, Truc; Kuhen, Kelli L.; Ellis, David Archer; Jiang, Tao
PATENT ASSIGNEE(S): IRM LLC, Bermuda
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037784	A2	20040506	WO 2003-US33560	20031021
WO 2004037784	A3	20040819		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003285952	A1	20040513	AU 2003-285952	20031021
US 2004157859	A1	20040812	US 2003-690873	20031021
PRIORITY APPLN. INFO.:			US 2002-420480P P	20021021
			US 2002-422619P P	20021030
			WO 2003-US33560 W	20031021

OTHER SOURCE(S): MARPAT 140:391194
GI

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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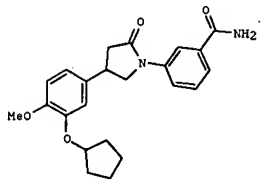
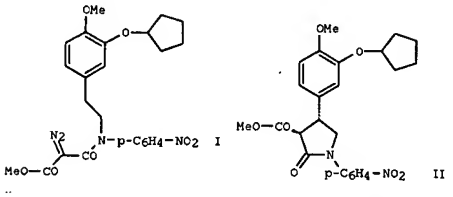


II

AB The present invention relates to inhibition of viruses, e.g., HIV using pyrrolidones I and compds. related to pyrrolidones I [R1 = H, alkyl, cycloalkyl; R2 = (un)substituted Ph, CH2Ph, cycloalkyl; R3 = (un)substituted pyridyl, pyrimidinyl, pyrazinyl, Ph]. The invention further relates to methods for identifying and using agents, including small mol. chemical compns. that inhibit HIV replication in a cell, as well as to methods of prophylaxis, and therapy related to HIV infection and related disease states such as AIDS. Preparation of the compds. I is described in 28 synthetic examples. Thus, reacting 4-(3-cyclopentyloxy-4-methoxyphenyl)-pyrrolidin-2-one with 3-bromobenzonitrile in the presence of potassium phosphate and trans-1,2-cyclohexanediamine in DMF/dioxane followed by treating a solution of the resulting benzonitrile with 25% NaOH solution, and then with 35% H2O2 afforded II.

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:584505 CAPLUS
DOCUMENT NUMBER: 135:344336
TITLE: Synthesis and structure-activity relationship of N-arylrolipram derivatives as inhibitors of PDE4 isozymes
AUTHOR(S): Keller, Thomas H.; Bray-French, Katharine; Demnitz, F. W. Joachim; Muller, Thomas; Pombo-Villar, Esteban; Walker, Christoph
CORPORATE SOURCE: Respiratory Disease Therapeutic Area, Novartis Horsham Research Center, West Sussex, RH12 5AB, UK
SOURCE: Chemical & Pharmaceutical Bulletin (2001), 49(8), 1009-1017
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:344336
AB Structure activity studies of N-phenylrolipram derivs. led to the identification of highly potent PDE4 inhibitors. The potential of these inhibitors for cellular activity was routinely assessed in an assay of fMLP induced oxidative burst in human eosinophils. Since 1st generation PDE4 inhibitors were plagued with a number of unwanted side effects, parallel structure activity studies for competition with the [3H]-rolipram binding site in rat brain were performed. In this fashion 5-[4-(3-cyclopentyloxy-4-methoxyphenyl)-2-oxopyrrolidin-1-yl]-3-(3-methoxybenzyloxy)benzoic acid N',N'-dimethylhydrazide was identified as a potent inhibitor of PDE4 which exhibits >1000 fold selectivity vs. PDE3, and is a nanomolar inhibitor in all the cellular assays tested. Studies on the stereoselectivity of PDE4 inhibition of this class of rolipram based compds. revealed, that for example (S)-4-(3-cyclopentyloxy-4-methoxyphenyl)-1-[-3-(3-methoxybenzyloxy)phenyl]pyrrolidin-2-one is a more potent inhibitor than the (R)-enantiomer. This effect can also be observed in primary human cells where the (S)-enantiomer is .apprx.10 fold more potent than the corresponding (R)-enantiomer.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:726410 CAPLUS
DOCUMENT NUMBER: 132:122469
TITLE: Catalytic enantioselective synthesis of the phosphodiesterase type IV inhibitor (R)-(-)-rolipram via intramolecular C-H insertion process
AUTHOR(S): Anada, Masahiro; Mita, Orie; Watanabe, Hiroko; Kitagaki, Shinji; Hashimoto, Shunichi
CORPORATE SOURCE: Graduate School Pharmaceutical Sciences, Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Synlett (1999), (11), 1775-1777
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:122469
GI



I II

AB A new route to (R)-(-)-rolipram was developed, wherein the key step relies on enantioselective intramol. C-H insertion of N-alkyl-N-(4-nitrophenyl)-α-(methoxycarbonyl)-α-diazoacetamide I catalyzed by a chiral dirhodium(II) complex. A dirhodium(II) carboxylate incorporating N-benzene-fused (S)-phthaloyl-tert-leucinate as a bridging ligand proved to be the catalyst of choice for this process, providing the desired 2-pyrrolidinone II in 88% ee.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:11369 CAPLUS
DOCUMENT NUMBER: 130:153528
TITLE: Synthesis of N-arylrolipram derivatives - potent and selective phosphodiesterase-IV inhibitors - by copper catalyzed lactam-aryl halide coupling
AUTHOR(S): Aebischer, Esther; Bacher, Edmond; Demnitz, F. W. Joachim; Keller, Thomas H.; Kurzmeyer, Miriam; Ortiz, Marta L.; Pombo-Villar, Esteban; Weber, Hans-Peter
CORPORATE SOURCE: NOVARTIS Pharma AG, Preclinical Research, Basel, CH-4002, Switz.
SOURCE: Heterocycles (1998), 48(11), 2225-2229
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:153528
AB The copper catalyzed coupling of rolipram with a wide variety of aryl halides affords N-arylrolipram derivs., potent and selective phosphodiesterase type-IV inhibitors.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:1280 CAPLUS
DOCUMENT NUMBER: 130:177372
TITLE: N-Arylrolipram derivatives as potent and selective PDE4 inhibitors
AUTHOR(S): Bacher, Edmond; Boer, Christiene; Bray-French, Katharine; Demnitz, F. W. Joachim; Keller, Thomas H.; Mazzoni, Lazzaro; Muller, Thomas; Walker, Christoph
CORPORATE SOURCE: Respiratory Disease Therapeutic Area, Novartis Horsham Research Center, West Sussex, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(22), 3229-3234
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Derivatization of rolipram led to the identification of 3-[4-(3-cyclopentyloxy-4-methoxyphenyl)-2-oxo-pyrrolidin-1-yl]-5-(3-methoxybenzyloxy)benzoic acid N',N'-dimethylhydrazide, a potent and selective inhibitor of PDE4, which inhibits the activation of human leukocytes with pIC50 values in the range of 7.3-7.8, and blocks antigen-induced eosinophilia in Brown Norway rats at a dose of 1 mg/kg.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 16 5-8 ibib abs hitstr

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

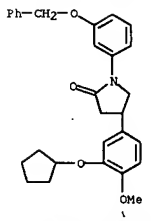
ACCESSION NUMBER: 2001:584505 CAPLUS
DOCUMENT NUMBER: 135:344336
TITLE: Synthesis and structure-activity relationship of N-arylrolipram derivatives as inhibitors of PDE4 isozymes
AUTHOR(S): Keller, Thomas H.; Bray-French, Katharine; Demnitz, F. W. Joachim; Muller, Thomas; Pombo-Villar, Esteban; Walker, Christoph
CORPORATE SOURCE: Respiratory Disease Therapeutic Area, Novartis Horsham Research Center, West Sussex, RH12 5AB, UK
SOURCE: Chemical & Pharmaceutical Bulletin (2001), 49(8), 1009-1017
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:344336

AB Structure activity studies of N-phenylrolipram derivs. led to the identification of highly potent PDE4 inhibitors. The potential of these inhibitors for cellular activity was routinely assessed in an assay of fMLP induced oxidative burst in human eosinophils. Since 1st generation PDE4 inhibitors were plagued with a number of unwanted side effects, parallel structure activity studies for competition with the [3H]-rolipram binding site in rat brain were performed. In this fashion 5-[4-(3-cyclopentyloxy-4-methoxyphenyl)-2-oxopyrrolidin-1-yl]-3-(3-methoxybenzyloxy)benzoic acid N',N'-dimethylhydrazide was identified as a potent inhibitor of PDE4 which exhibits >1000 fold selectivity vs. PDE3, and is a nanomolar inhibitor in all the cellular assays tested. Studies on the stereoselectivity of PDE4 inhibition of this class of rolipram based compds. revealed, that for example (S)-4-(3-cyclopentyloxy-4-methoxyphenyl)-1-[-3-(3-methoxybenzyloxy)phenyl]pyrrolidin-2-one is a more potent inhibitor than the (R)-enantiomer. This effect can also be observed in primary human cells where the (S)-enantiomer is .apprx.10 fold more potent than the corresponding (R)-enantiomer.

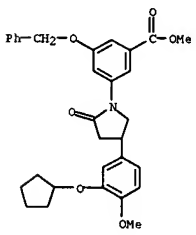
IT 220284-70-8P 220284-76-4P 220284-92-4P
220573-56-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and structure-activity relationship of N-arylrolipram derivs. as inhibitors of PDE4 isoenzymes)

RN 220284-70-8 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

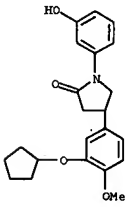
L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 220284-76-4 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

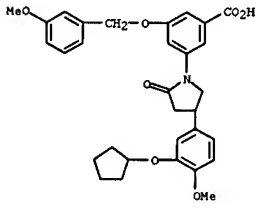


RN 220284-92-4 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)



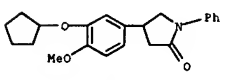
L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 220573-56-8 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-[(3-methoxyphenyl)methoxy]- (9CI) (CA INDEX NAME)



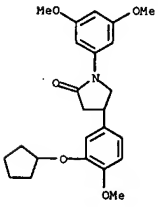
IT 220284-63-9P 220284-64-0P 220284-72-0P
220284-74-2P 220284-93-5P 220284-96-8P
220284-97-9P 220573-55-7P 220573-58-0P
371755-05-4P 371755-06-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and structure-activity relationship of N-arylrolipram derivs. as inhibitors of PDE4 isoenzymes)

RN 220284-63-9 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-phenyl- (9CI) (CA INDEX NAME)



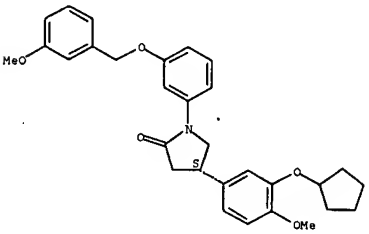
RN 220284-64-0 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



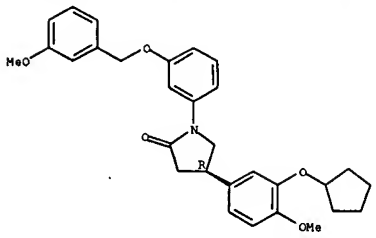
RN 220284-72-0 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(3-methoxyphenyl)methoxy]phenyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

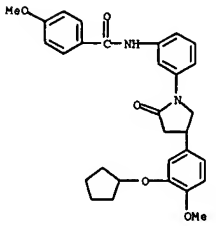


RN 220284-74-2 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(3-methoxyphenyl)methoxy]phenyl]-, (4R)- (9CI) (CA INDEX NAME)

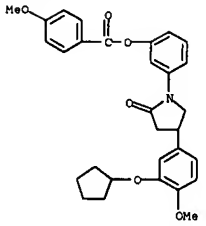
Absolute stereochemistry. Rotation (-).



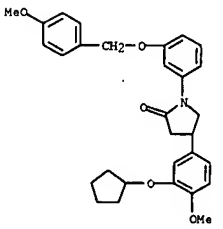
RN 220284-93-5 CAPLUS
CN Benzamide, N-[3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]phenyl]-4-methoxy- (9CI) (CA INDEX NAME)



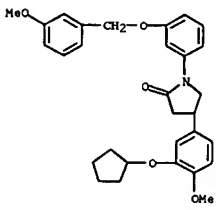
RN 220284-96-8 CAPLUS
CN Benzoic acid, 4-methoxy-, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]phenyl ester (9CI) (CA INDEX NAME)



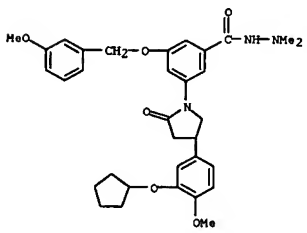
RN 220284-97-9 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(4-methoxyphenyl)methoxy]phenyl]- (9CI) (CA INDEX NAME)



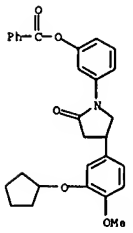
RN 220573-55-7 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(3-methoxyphenyl)methoxy]phenyl]- (9CI) (CA INDEX NAME)



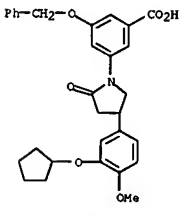
RN 220573-58-0 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-[(3-methoxyphenyl)methoxy]-, 2,2-dimethylhydrazide (9CI) (CA INDEX NAME)



RN 371755-05-4 CAPLUS
CN 2-Pyrrolidinone, 1-[3-(benzoyloxy)phenyl]-4-[3-(cyclopentyloxy)-4-methoxyphenyl]- (9CI) (CA INDEX NAME)

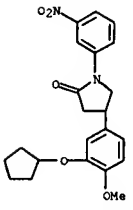


RN 371755-06-5 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

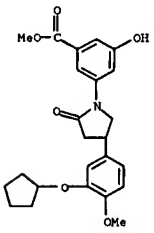


IT 220284-84-4P 220573-59-1P 220573-60-4P
371755-04-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and structure-activity relationship of N-arylrolipram derivs. as inhibitors of PDE4 isoenzymes)

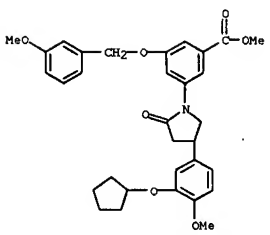
RN 220284-84-4 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



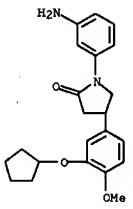
RN 220573-59-1 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



RN 220573-60-4 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-[(3-methoxyphenyl)methoxy]-, methyl ester (9CI) (CA INDEX NAME)

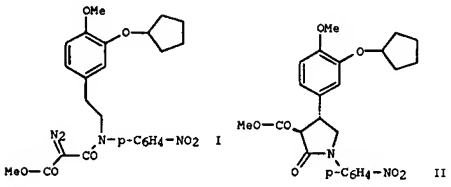


RN 371755-04-3 CAPLUS
CN 2-Pyrrolidinone, 1-(3-aminophenyl)-4-[3-(cyclopentyloxy)-4-methoxyphenyl]- (9CI) (CA INDEX NAME)



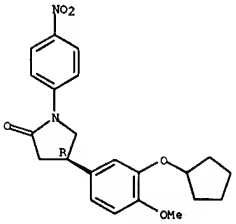
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:726410 CAPLUS
DOCUMENT NUMBER: 132:122469
TITLE: Catalytic enantioselective synthesis of the phosphodiesterase type IV inhibitor (R)-(-)-rolipram via intramolecular C-H insertion process
AUTHOR(S): Anada, Masahiro; Mita, Orie; Watanabe, Hiroko; Kitagaki, Shinji; Hashimoto, Shunichi
CORPORATE SOURCE: Graduate School Pharmaceutical Sciences, Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Synlett (1999), (11), 1775-1777
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:122469
GI



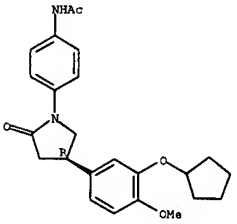
AB A new route to (R)-(-)-rolipram was developed, wherein the key step relies on enantioselective intramol. C-H insertion of N-alkyl-N-(4-nitrophenyl)-α-(methoxycarbonyl)-α-diazoacetamide I catalyzed by a chiral dirhodium(II) complex. A dirhodium(II) carboxylate incorporating N-benzene-fused (S)-phthaloyl-tert-leucinate as a bridging ligand proved to be the catalyst of choice for this process, providing the desired 2-pyrrolidinone II in 88% ee.
IT 256399-07-2P 256399-08-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of rolipram via intramol. C-H insertion)
RN 256399-07-2 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(4-nitrophenyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 256399-08-3 CAPLUS
CN Acetamide, N-[4-[(4R)-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

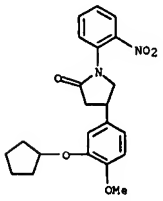
L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:11369 CAPLUS
DOCUMENT NUMBER: 130:153528
TITLE: Synthesis of N-arylrolipram derivatives - potent and selective phosphodiesterase-IV inhibitors - by copper catalyzed lactam-aryl halide coupling
AUTHOR(S): Aebischer, Esther; Bacher, Edmond; Demnitz, F. W. Joachim; Keller, Thomas H.; Kurzmeyer, Miriam; Ortiz, Marta L.; Pombo-Villar, Esteban; Weber, Hans-Peter
CORPORATE SOURCE: NOVARTIS Pharma AG, Preclinical Research, Basel, CH-4002, Switz.
SOURCE: Heterocycles (1998), 48(11), 2225-2229
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:153528

AB The copper catalyzed coupling of rolipram with a wide variety of aryl halides affords N-arylrolipram derivs., potent and selective phosphodiesterase type-IV inhibitors.

IT 220284-66-2P 220284-70-8P 220284-84-4P
220284-86-6P 220284-88-8P 220284-92-4P
220284-94-6P 220284-99-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylroliprams by copper-catalyzed coupling reaction of rolipram)

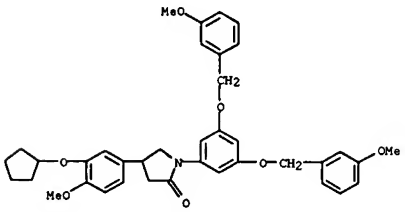
RN 220284-66-2 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(2-nitrophenyl)- (9CI) (CA INDEX NAME)



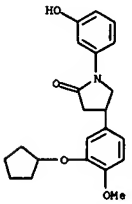
RN 220284-70-8 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CN 2-Pyrrolidinone, 1-[3,5-bis[(3-methoxyphenyl)methoxy]phenyl]-4-[3-(cyclopentyloxy)-4-methoxyphenyl]- (9CI) (CA INDEX NAME)



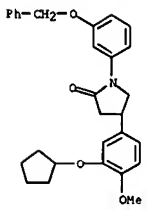
RN 220284-92-4 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)



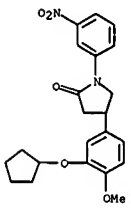
RN 220284-94-6 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(1E)-2-(4-methoxyphenyl)ethenyl]phenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

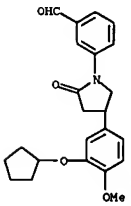
L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 220284-84-4 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3-nitrophenyl)- (9CI) (CA INDEX NAME)

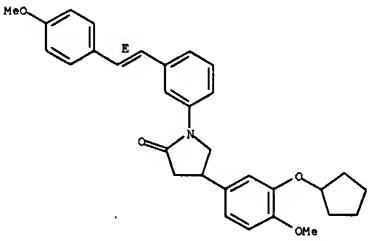


RN 220284-86-6 CAPLUS
CN Benzaldehyde, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

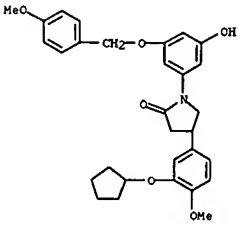


RN 220284-88-8 CAPLUS

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

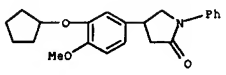


RN 220284-99-1 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-hydroxy-5-[(4-methoxyphenyl)methoxy]phenyl]- (9CI) (CA INDEX NAME)

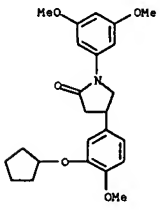


IT 220284-63-9P 220284-64-0P 220284-65-1P
220284-67-3P 220284-68-4P 220284-69-5P
220284-72-0P 220284-74-2P 220284-76-4P
220284-82-2P 220284-90-2P 220284-91-3P
220284-93-5P 220284-95-7P 220284-96-8P
220284-97-9P 220284-98-0P 220285-00-7P
220285-01-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of arylroliprams by copper-catalyzed coupling reaction of rolipram)

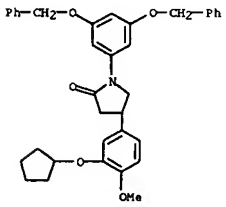
RN 220284-63-9 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-phenyl- (9CI) (CA INDEX NAME)



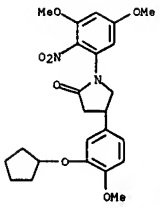
RN 220284-64-0 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



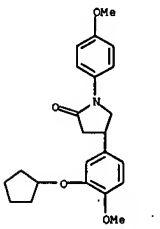
RN 220284-65-1 CAPLUS
CN 2-Pyrrolidinone, 1-[3,5-bis(phenylmethoxy)phenyl]-4-[3-(cyclopentyloxy)-4-methoxyphenyl]- (9CI) (CA INDEX NAME)



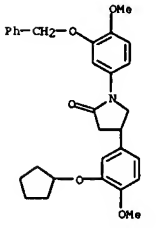
RN 220284-67-3 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3,5-dimethoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 220284-68-4 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

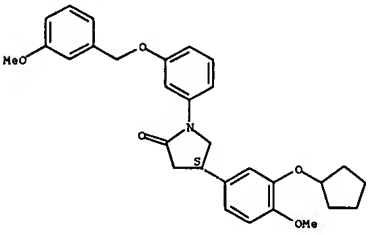


RN 220284-69-5 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[4-methoxy-3-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



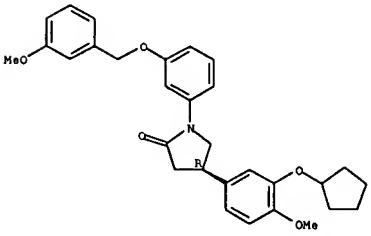
RN 220284-72-0 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(3-methoxyphenyl)methoxy]phenyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

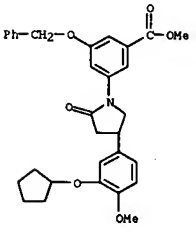


RN 220284-74-2 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(3-methoxyphenyl)methoxy]phenyl]-, (4R)- (9CI) (CA INDEX NAME)

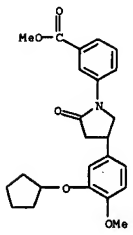
Absolute stereochemistry. Rotation (-).



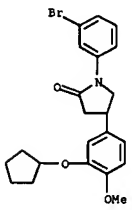
RN 220284-76-4 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)



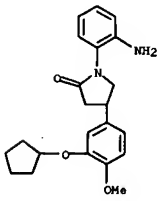
RN 220284-82-2 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-, methyl ester (9CI) (CA INDEX NAME)

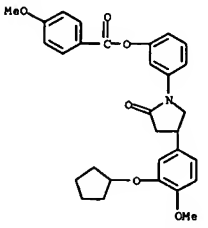


RN 220284-90-2 CAPLUS
CN 2-Pyrrolidinone, 1-(3-bromophenyl)-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-
(9CI) (CA INDEX NAME)

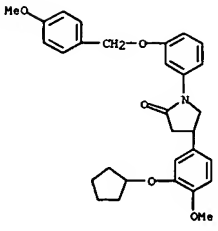


RN 220284-91-3 CAPLUS
CN 2-Pyrrolidinone, 1-(2-aminophenyl)-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-
(9CI) (CA INDEX NAME)



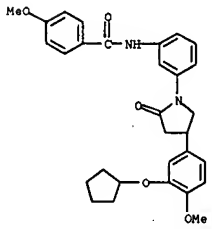


RN 220284-97-9 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(4-
methoxyphenyl)methoxy]phenyl]- (9CI) (CA INDEX NAME)

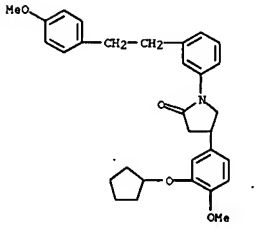


RN 220284-98-0 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[2-(3,4-
dimethoxyphenyl)-2-oxoethoxy]phenyl]- (9CI) (CA INDEX NAME)

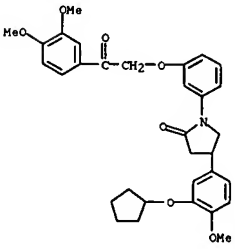
RN 220284-93-5 CAPLUS
CN Benzamide, N-[3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-
pyrrolidinyl]phenyl]-4-methoxy- (9CI) (CA INDEX NAME)



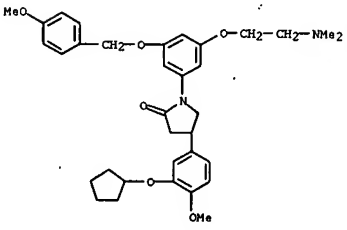
RN 220284-95-7 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[2-(4-
methoxyphenyl)ethyl]phenyl]- (9CI) (CA INDEX NAME)



RN 220284-96-8 CAPLUS
CN Benzoic acid, 4-methoxy-, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-
1-pyrrolidinyl]phenyl ester (9CI) (CA INDEX NAME)



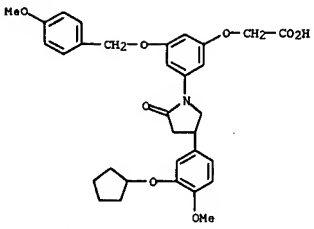
RN 220285-00-7 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[2-
(dimethylamino)ethoxy]-5-[(4-methoxyphenyl)methoxy]phenyl]-,
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 220285-01-8 CAPLUS
CN Acetic acid, [3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-
pyrrolidinyl]-5-[(4-methoxyphenyl)methoxy]phenoxy]- (9CI) (CA INDEX NAME)

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

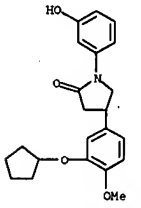
L6 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:1280 CAPLUS
DOCUMENT NUMBER: 130:177372
TITLE: N-Arylrolipram derivatives as potent and selective PDE4 inhibitors
AUTHOR(S): Bacher, Edmond; Boer, Christiens; Bray-French, Katharine; Demnitz, F. W. Joachim; Keller, Thomas H.; Mazzoni, Lazzaro; Muller, Thomas; Walker, Christoph
CORPORATE SOURCE: Respiratory Disease Therapeutic Area, Novartis Horsham Research Center, West Sussex, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(22), 3229-3234
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Derivatization of rolipram led to the identification of 3-[4-(3-cyclopentyloxy-4-methoxyphenyl)-2-oxo-pyrrolidin-1-yl]-5-(3-methoxybenzyloxy)benzoic acid N',N'-dimethylhydrazide, a potent and selective inhibitor of PDE4, which inhibits the activation of human leukocytes with pIC50 values in the range of 7.3-7.8, and blocks antigen-induced eosinophilia in Brown Norway rats at a dose of 1 mg/kg.

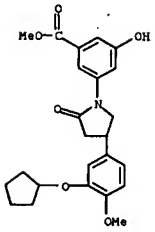
IT 220284-92-4P 220573-59-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(alkylation; preparation of arylrolipram derivs. as selective PDE4 inhibitors)

RN 220284-92-4 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)



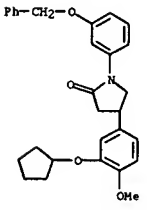
RN 220573-59-1 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



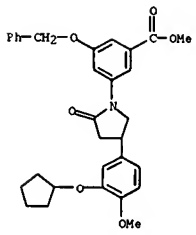
IT 220284-70-8P 220284-76-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydrogenolysis; preparation of arylrolipram derivs. as selective PDE4 inhibitors)

RN 220284-70-8 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



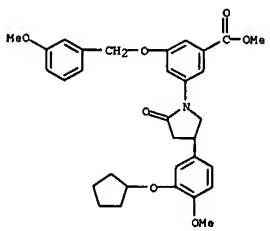
RN 220284-76-4 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



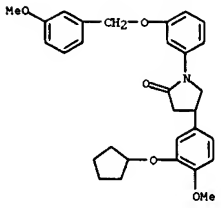
IT 220573-60-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydrolysis; preparation of arylrolipram derivs. as selective PDE4 inhibitors)

RN 220573-60-4 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-[(3-methoxyphenyl)methoxy]-, methyl ester (9CI) (CA INDEX NAME)

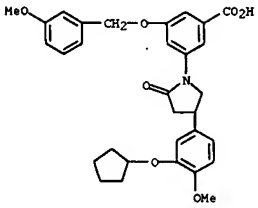


IT 220573-55-7P 220573-56-8P 220573-58-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of arylrolipram derivs. as selective PDE4 inhibitors)

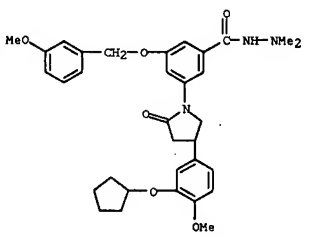
RN 220573-55-7 CAPLUS
CN 2-Pyrrolidinone, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[3-[(3-methoxyphenyl)methoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 220573-56-8 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-[(3-methoxyphenyl)methoxy]- (9CI) (CA INDEX NAME)

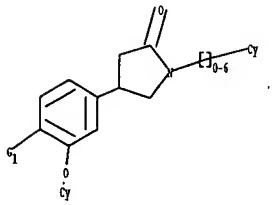


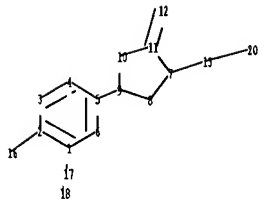
RN 220573-58-0 CAPLUS
CN Benzoic acid, 3-[4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]-5-[(3-methoxyphenyl)methoxy]-, 2,2-dimethylhydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Uploading C:\Program Files\Stnexp\Queries\10690873b.str





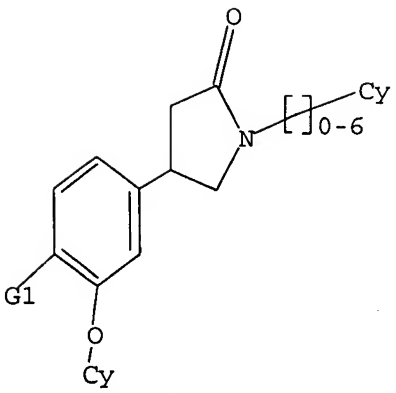
chain nodes :
12 13 16 17 18 20
ring nodes :
1 2 3 4 5 6 7 8 9 10 11
chain bonds :
1-17 2-16 5-9 7-13 11-12 13-20 17-18
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11
exact/norm bonds :
1-17 2-16 7-8 7-11 7-13 8-9 9-10 10-11 11-12 13-20 17-18
exact bonds :
5-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:H,X,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,PhO,CN,Ak

Hydrogen count :
8:>= minimum 2 10:>= minimum 2
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 16:CLASS 17:CLASS 18:Atom 20:Atom

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 H,X,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,PhO,CN,Ak

Structure attributes must be viewed using STN Express query preparation.

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=> s l1 full
FULL SEARCH INITIATED 17:03:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    31410 TO ITERATE

100.0% PROCESSED    31410 ITERATIONS                          661 ANSWERS
SEARCH TIME: 00.00.01

L2          661 SEA SSS FUL L1

=> d l2 1-10
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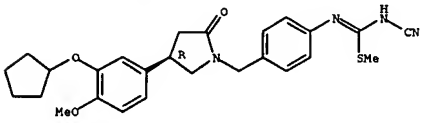
L2 ANSWER 1 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 916057-20-0 REGISTRY
ED Entered STN: 20 Dec 2006
CN Carbamimidothioic acid, N-cyano-N'-[4-[[(4R)-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-oxo-1-pyrrolidinyl]methyl]phenyl]-, methyl ester (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H30 N4 O3 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

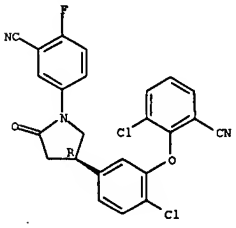


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-13-5 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 3-chloro-2-[2-chloro-5-[(3R)-1-(3-cyano-4-fluorophenyl)-5-oxo-3-pyrrolidinyl]phenoxy]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H14 Cl2 F N3 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

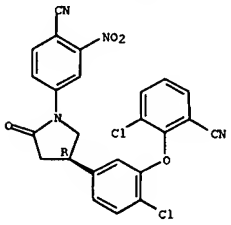


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-10-2 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 3-chloro-2-[2-chloro-5-[(3R)-1-(4-cyano-3-nitrophenyl)-5-oxo-3-pyrrolidinyl]phenoxy]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H14 Cl2 N4 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

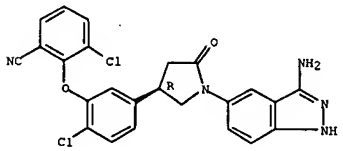


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 4 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-09-9 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 2-[5-[(3R)-1-(3-amino-1H-indazol-5-yl)-5-oxo-3-pyrrolidinyl]-2-chlorophenoxy]-3-chloro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H17 Cl2 N5 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

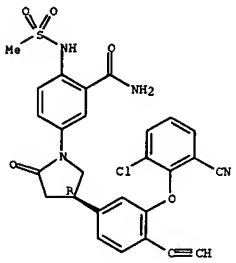


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 5 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-08-8 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H21 Cl N4 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

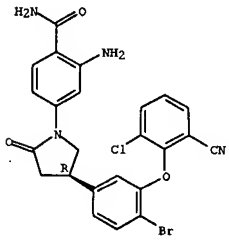


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 6 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-07-7 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 2-amino-4-[(4R)-4-[4-bromo-3-(2-chloro-6-cyanophenoxy)phenyl]-2-oxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H18 Br Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

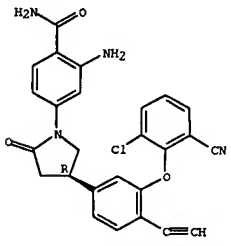


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 7 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-06-6 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 2-amino-4-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H19 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

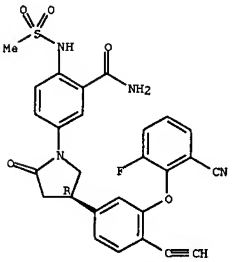


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 8 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-05-5 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-cyano-6-fluorophenoxy)-4-ethynylphenyl]-2-oxo-1-pyrrolidinyl]-2-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H21 F N4 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

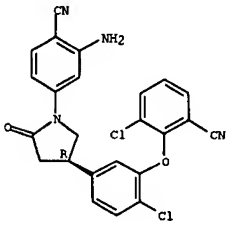


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 9 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-04-4 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzonitrile, 2-[5-[(3R)-1-(3-amino-4-cyanophenyl)-5-oxo-3-pyrrolidinyl]-2-chlorophenoxy]-3-chloro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H16 Cl2 N4 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

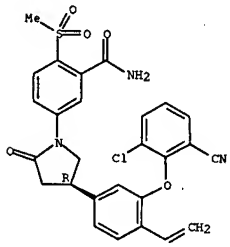


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 10 OF 661 REGISTRY COPYRIGHT 2007 ACS on STN
RN 903579-03-3 REGISTRY
ED Entered STN: 23 Aug 2006
CN Benzamide, 5-[(4R)-4-[3-(2-chloro-6-cyanophenoxy)-4-ethenylphenyl]-2-oxo-1-pyrrolidinyl]-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H22 Cl N3 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)